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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,695	01/30/2004	Shubh D. Sharma	70025-US04-129	8611

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/769,695	SHARMA ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above claim(s) *34-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-9 (in part) and 10-21 and species of receptor in the response filed May 30, 2006 is acknowledged. The traversal is on the ground(s) that Group I and Group II would not require different searches, thus there is no serious search burden on the Examiner to include Group II. Regarding the species election, since the invention of claims 1 and 10 are directed to a "parent polypeptide", the invention differs as to the asserted species only as to the target or the classification of the binding partner for the parent polypeptide, it is unlikely an individual search would be fruitful. Applicants' response has been considered, and the arguments are not found persuasive regarding Groups I and II, and species election, thus Group II will be examined along with Group I, and the requirement for the election of single species is withdrawn. Therefore, claims 1-33 are examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 1-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of determining the specific residues binding to a target of interest such as a receptor within a known parent polypeptide that binds to the target of interest, the method comprising the steps of: (a) providing a known parent polypeptide with primary structure consisting of n residues, where n is 3 to 20 amino acid residues; (b) constructing a first peptide of R_1-Z-R_2 with R_1 being 2 to n-2 residues, Z being an amino acid residue having both an

N and an S for metal ion complexation, and R_2 being 0 to n-2 residues, where the amino acid residues in R_1 or R_2 are the same as the residues in the parent peptide, and Z is inserted into the primary structure or substituting for a single residue in the primary structure; (c) complexing the peptide of R_1-Z-R_2 to a metal ion and forming R_1-Z-R_2 metallopeptide, where metal ion is Re or Tc,; (d) screening R_1-Z-R_2 metallopeptide for binding to the receptor as the target of interest; (e) repeating steps (b) through (d), wherein the resulting R_1-C-R_2 metallopeptide differs in at least either R_1 or R_2; and (f) selecting the R_1-Z-R_2 metallopeptide exhibiting decreased binding to the target of interest, does not reasonably provide enablement for a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest, the method comprising the steps of: (a) providing a known parent polypeptide with primary structure consisting of n residues; (b) constructing a first peptide of R_1-Z-R_2 with R_1, Z, R_2 each defined in claim 1; (c) complexing the peptide of R_1-Z-R_2 to a metal ion and forming R_1-Z-R_2 metallopeptide; (d) screening R_1-Z-R_2 metallopeptide for binding to the target of interest; (e) repeating steps (b) through (d), wherein the resulting R_1-Z-R_2 metallopeptide differs in at least either R_1 or R_2; and (f) selecting the R_1-Z-R_2 metallopeptide exhibiting decreased binding to the target of interest, or the method comprising the steps of making a series of peptides including the known primary sequences of the parent polypeptide and a single L- or D-3-mercapto amino acid residue inserted between the two positions (starting at the second and third positions) or substituting at each residue (starting at the third residue) of the primary sequence, complexing each peptide in the series with a metal ion, and determining the binding of each metallopeptide to the target of interest, where the "n" or the length of the parent polypeptide and the metal ion are not defined, the amino acid residues in R_1 or R_2 are

homologs of the residues in the parent peptide, and Z is a mimetic of a residue having both an N and an S without defined structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-33 encompass a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest. The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the present invention provides a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest by constructing a peptide of R_1-Z-R_2, complexing the peptide of R_1-Z-R_2 to a metal ion forming R_1-Z-R_2 metallopeptide, and screening R_1-Z-R_2 metallopeptide for binding to the target of interest (pages 5-8). There are no indicia that the present application enables the full scope in view of the claimed method using the R_1-Z-R_2 metallopeptide as discussed in the stated rejection. The present application does not provide sufficient teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the metal ions, the n residues, the amino acid residues in R_1 or R_2 being homologs of the residues of the parent peptide, and Z being a residue or mimetic having both an N and an S without defined structure, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Examples 1-12 describe the Re complex of a specific peptide sequence that binds to specific receptor, e.g., Re peptide of α-MSH with L-Cys or D-Cys insertion in binding to Melanocortin receptor (Examples 1-2); Re peptide of [Nle^3, D-Phe^6] γ-MSH or [Nle^3] γ-MSH with L-Cys insertion in binding to Melanocortin receptor (Examples 3-4); Re peptide of [Nle^3, D-Phe^6] γ-MSH with L-Cys substitution in binding to Melanocortin receptor (Example 5); and Bombesin or bombesin-like peptides with L-Cys insertion or substitution in binding bombesin receptor (Examples 6-12). The examples illustrate the parent peptides with 9-14 residues but do not provide sufficient teachings on the R_1-Z-R_2 peptides with n being more than 20 residues and amino acid residues being homologs of the residues of the parent peptide, and Z being a residue or mimetic having an N and an S for metal ion complexation.

(3). The state of the prior art and relative skill of those in the art:

The related art (references cited at pages 3-4, e.g., U.S. Patent 5,834,250) teach methods for systematic analysis of structure and function of polypeptides, specifically by identifying active domains by substituting a scanning amino acid for the amino acid residues within a suspected active domain of the parent polypeptide, but the methods do not provide direct information concerning the secondary structure of the active domain. Furthermore, the general knowledge and level of the skill in the art do not supplement the omitted description, the

specification needs to provide teachings on the longer peptides (e.g., n >20 residues) which may have tertiary structures other than secondary structures, where the tertiary structure may effect the binding of R_1-Z-R_2 to a metal ion and the binding of R_1-Z-R_2 metallopeptide to a target of interest.

(4). Predictability or unpredictability of the art:

The claims are directed to a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest, which encompasses numerous variants regarding parent peptides with undefined n residues and the amino acid residues in R_1 or R_2 being homologs of the residues in the parent peptide. While the specification provides Re peptides of several specific peptide sequences with defined n residues (n= 9-14) in binding specific receptors, the specification does not provide sufficient teachings in the amino acid residues in R_1 or R_2 being homologs of the residues of the parent peptide, and R_1-Z-R_2 peptides with n residues more than 20, where a tertiary structure may exist and affect the binding of R_1-Z-R_2 to a metal ion and the binding of R_1-C-R_2 metallopeptide to the target of interest. Furthermore, the specification merely describes "Z" being an amino acid having an N and an S for metal ion complexation, it does not indicate Z is a residue or mimetic thereof having an N and an S with an undefined structure, e.g., if amino and carboxyl groups are not present in "Z", how to make R_1-Z-R_2 without forming a peptide bond. Thus, the invention is highly unpredictable regarding the structure of the R_1-Z-R_2 metallopeptide with undefined "n" and homologs of residues, and binding of R_1-Z-R_2 metallopeptide having n> 20 to a target of interest.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest. The specification indicates Re peptides of specific peptide sequences that bind to specific receptors (Example 1-12), it does not provide sufficient teachings in the use of R_1-Z-R_2 peptides containing more than 20 residues, homologs of the residues in R_1-Z-R_2 formula and Z being a residue or mimetic having an N and an S, in forming metallopeptides with various metal ion in the claimed method. Moreover, there are no working examples demonstrating the claimed methods associated with various parent peptides that bind to various targets of interest. Since the specification does not provide sufficient teachings on the use of various R_1-Z-R_2 metallopeptides in the claimed methods, it is necessary to have additional guidance and to carry out undue experimentation to identify R_1-Z-R_2 metallopeptides that exhibit decreased binding to various targets of interest in the claimed method.

(6). Nature of the Invention

The scope of the claims encompasses a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest, but the specification does not demonstrate the use of various R_1-Z-R_2 metallopeptides containing undefined n residues, homologs of amino acid resides in R_1-Z-R_2 formula, Z being a residue or mimetic having an N and an S and various metal ions in binding various targets of interest. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working examples do not demonstrate the claimed methods associated with variants, the structure and effect of the R_1-Z-R_2 metallopeptide are unpredictable, and the teachings in the specification are limited, therefore, it

is necessary to have additional guidance and to carry out undue experimentation to identify the metallopeptides that exhibit decreased binding to various targets of interest.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 1-9, 11 and 23 are indefinite because of the use of the term "n residues", "mimetic thereof" or "substantially". The cited term renders the claim indefinite, it is not clear what are the metes and bounds for "n residues". It is also not clear what structure the mimetic of a residue has, and how different the mimetic is from the parent residue; and how much decrease in binding the term "substantially" refers to. Claims 2-9 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

5. Claims 10-33 are indefinite as to how the specific residues that binds to a target of interest in the primary sequence of parent polypeptide are determined. Claims 11-21 and 23-33 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 1-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5-40 and 42-76 of co-pending application No. 10/464,117 (based on the amended claims filed February 6, 2006). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-33 in the instant application disclose a method of determining the specific residues binding to a target of interest within a known parent polypeptide that binds to the target of interest, comprising the steps of: (a) providing a known parent polypeptide with primary structure consisting of n residues; (b) constructing a first peptide of R_1-Z-R_2 with R_1, Z, R_2 each defined; (c) complexing the peptide of R_1-Z-R_2 to a metal ion and forming R_1-Z-R_2 metallopeptide; (d) screening R_1-Z-R_2 metallopeptide for binding to the target of interest; (e) repeating steps (b) through (d), wherein the resulting R_1-Z-R_2 metallopeptide differs in at least either R_1 or R_2; and (f) selecting the R_1-Z-R_2 metallopeptide exhibiting substantially decreased binding to the target of interest; or comprising the steps of making a series of peptides including the known primary sequences of the parent polypeptide and a single L- or D-3-mercapto amino acid residue inserted between the two positions (starting the second and third positions) or substituting at each residue (starting the third residue) of the primary sequence, complexing each

peptide in the series with a metal ion, and determining the binding of each metallopeptide to the target of interest. This is obvious variation in view of claims 1-3, 5-40 and 42-76 in the co-pending application disclose a method of determining a secondary structure binding to a target of interest within a known parent polypeptide that binds to the target of interest, comprising the steps of: e.g., (a) providing a known parent polypeptide with primary structure consisting of n residues; (b) constructing a first peptide of R_1-C-R_2 with R_1, C, R_2 each defined; (c) complexing the peptide of R_1-C-R_2 to a metal ion and forming R_1-C-R_2 metallopeptide; (d) screening R_1-C-R_2 metallopeptide for binding to the target of interest; (e) repeating steps (b) through (d), wherein the resulting R_1-C-R_2 metallopeptide differs in at least either R_1 or R_2; and (f) selecting the R_1-C-R_2 metallopeptide exhibiting binding to the target of interest. Since both groups of claims are directed to a method of determining the secondary structure of the residues binding to a target of interest within a known parent polypeptide, thus, claims 1-33 in present application and claims 1-3, 5-40 and 42-76 in the co-pending application are obvious variations of a method of determining a secondary structure binding to a target of interest within a known parent polypeptide that binds to the target of interest.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
July 7, 2006